## REMARKS

Reconsideration of the Final Office Action mailed March 14, 2003, (hereinafter "instant Office Action"), entry of the foregoing amendments and withdrawal of the rejection of claims 18-21 and 23-45, are respectfully requested. Applicants respectfully request that the amendment filed with the Reply mailed August 14, 2003 not be entered.

In the instant Office Action, claims 18-21 and 23-45 are listed as pending, and claims 18-21 and 23-45 are listed as rejected. Claims 1-17 and 22 were previously withdrawn by the Examiner. Claim 40 has been withdrawn by the Applicants.

The Examiner has rejected claim 18 under 35 U.S.C. §102(b), for allegedly being anticipated by Hiremath et al. The Examiner alleges that claim 18 reads on compounds 8a-f and 13a-d on page 761 of Hiremath et al. Compounds 8a-f and 13a-d of Hiremath et al. have been provisoed out of Claim 18.

Based upon the foregoing, the rejection of claim 18 under 35 U.S.C. §102(b) over Hiremath et al. is obviated and should be withdrawn.

The Examiner has rejected claim 18 under 35 U.S.C. §102(b), for allegedly being anticipated by Mitra et al. The Examiner alleges that Mitra et al. teaches the compound with RN 68761-49-9 which corresponds to the compound of the instant claim when in the instant case $R^1$ is methyl and R is phenyl. Applicants have amended claim 18 to proviso out the compound of Formula (II) of Mitra, where $R_1$ is phenyl and $R_b$ is H.

Based upon the foregoing, the rejection of claim 18 under 35 U.S.C. §102(b) over Mitra et al. is obviated and should be withdrawn.

The Examiner has rejected claim 18 under 35 U.S.C. §103(a) as allegedly being unpatentable over Blum et al. (US 6,074,878). The Examiner alleges that the reference teaches the compound of example 10 and that the claim differs by having a hydrogen over the prior art methyl on the ring nitrogen of the pyrazolinone. Applicants respectfully traverse this rejection.

### BASIC REQUIREMENTS OF A *PRIMA FACIE* CASE OF OBVIOUSNESS

> To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all claim limitations.

The Examiner has not established a *prima facie* case of obviousness. The reference does not provide any suggestion or motivation to modify Blum et al. to arrive at Applicants' genus. Second, there must be a reasonable expectation of success. Blum et al. is directed to use of compounds as dyes, whereas the instant application is directed to compounds and their use as inhibitors of protein kinase activity, an entirely different and unrelated use. One of ordinary skill in the art of medicinal chemistry would not expect a dye to be an effective inhibitor of protein kinase activity. Applicants respectfully direct the Examiner's attention to In re Oetiker, 24 USPQ2d 1443 (1992), wherein the Court of Appeals for the Federal Circuit stated that:

> In order to rely on a reference as a basis for rejection of the applicant's invention, the reference must either be in the field of the applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the inventor was concerned.

In re Oetiker, 24 USPQ2d at 1445.

Applicants' compounds have a completely different use than the compounds in Blum et al., i.e. kinase inhibitors as opposed to dyes. Therefore, one of ordinary skill in the art would not be motivated to look to Blum for a suggestion of Applicants' Claim 18, since the two subject matters are in such divergent fields.

The Court of Appeals for the Federal Circuit has stated the following on the issue of obviousness:

> Uniroyal, Inc. v. Rudkin-Wiley Corp., 837 F. 2d 1044, 1051-52, 5 USPQ 1434, 1438 (Fed. Cir. 1988), cert. denied, 109 S. Ct. 75 (1988), on remand, 13 USPQ2d 1192 (D. Conn. 1989) "Something in the prior art as a whole must suggest the desirability, and thus the obviousness, of making the combination."; In re Stencel, 828 F. 2d 751,755, 4 USPQ2d 1071, 1073 (Fed. Cir. 1987) obviousness cannot be established "by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion that the combination be made."' Alco Standard Corp. v. Tennessee Valley Authority, 808 F. 2d 1490, 1498, 1 USPQ2d 1337, 1343 (Fed. Cir. 1986), cert. dismissed, 108 S. Ct. 26 (1987) "the question is not simply whether the prior art 'teaches' the particular element of the invention, but whether it would 'suggest the desirability, and thus the obviousness, of making the combination.'"; Carella v. Starlight Archery, 804 F. 2d 135,231 USPQ 644 (Fed. Cir. 1986); ACS Hospital Sys., Inc. v. Montefiore Hospital, 732 F. 2d 1572, 221 USPQ 929 (Fed. Cir. 1984) "Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination. Under section 103, teachings of references can be combined only if there is some suggestion or incentive to do so."

Donald S. Chisum, Patents, A Treatise on the Law of Patentability, Validity and Infringement, Vol. 2, 5-218, 1992.

Blum et al. does not teach or suggest all of the limitations of Applicants' claims. The Examiner alleges that with respect to example 10 of Blum et al., Applicants' compound differs by having a hydrogen over the prior art methyl on the ring nitrogen of the pyrazolinone. With respect to motivation or suggestion within the reference itself to modify the reference so that it would encompass Applicants' invention, the Examiner cites Ex Parte Weston and Hamlin 121 USPQ 428, Ex parte Bluestone and In re Doebel stating that these cases "affirm that NCH3 is obvious over N-H." The Examiner also cites In re Hoeksema, 154 USPQ 169 "...a chemist looking at the formula for another compound which differs so slightly that it is called a homolog generally expects the second compound to have properties similar to the first one." Applicants respectfully point out that Blum et al. is directed to dyes, whereas the instant application is directed to therapeutic agents. Blum et al. is nonanalogous art. One skilled in the art of medicinal chemistry would not look to the field of dyes for therapeutics. Blum et al. does not suggest or teach the genus in Applicants' Claim 18.

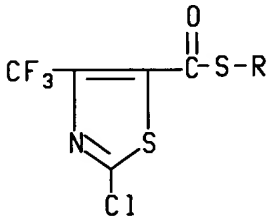
To establish a *prima facie* case of obviousness, the invention must be considered as a whole, there must be some suggestion or motivation to modify the reference, the reference must teach or suggest all of the claim limitations and there must be a reasonable chance of success.
The Examiner alleges that "The reference teaches the compound of example 10 (see cols 13-14). The claim differs by having a hydrogen over the prior art methyl on the ring nitrogen of the pyrazolinone." However, an invention is to be considered as a whole. That is, in this case, does Blum et al. make obvious the entire genus of any of Applicants' claims? The claimed invention may not be dissected into discrete elements to be analyzed in isolation, but must be considered as a whole. See, e.g. W.L. Gore & Assoc. Inc. v. Garlock, Inc. 721 F.2d 1540, 1548, 220 USPQ 303, 309 (Fed. Cir. 1983)); Jones v. Hardy, 727 F.2d 1524, 1530, 220 USPQ 1021, 1026 (Fed. Cir. 1983). In determining the differences between the prior art and the claims, the question under 35 U.S.C. §103 is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious. Stratoflex, Inc. v. Aeroquip Corp., 713 F.2d 1530, 218 USPQ 871 (Fed. Cir. 1983); Schenck v. Nortron Corp.,713 F.2d 782, 218 USPQ 698 (Fed. Cir. 1983). The Examiner has not shown how Blum et al. renders obvious the entire genus of Applicants' claim. Further, Blum et al. does not teach or suggest all of the limitations of Applicants' claim. As stated in M.P.E.P. 2143.03, "To establish prima facie obviousness of a

claimed invention, all of the claim limitations must be taught or suggested by the prior art." In re Royka, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Applicants maintain that Blum et al. does not render claim 18 obvious.

Even in a case where the structural similarity was close, the CAFC has stated that a definite suggestion is needed in order to make the modification to establish a *prima facie* case of obviousness. In In re Grabiak the CAFC stated that "there must be adequate support in the prior art for the ester/thioester change in structure, in order to complete the PTO's prima facie case and shift the burden of going forward to the applicant." In re Grabiak, 226 USPQ 870, 872, 1985.

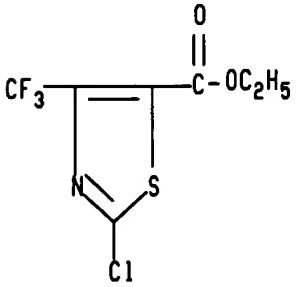
The Grabiak court made the above statement in light of the fact that both appellant's compounds and the prior art compounds were very similar in structure (see below) and had the same utility, namely, as herbicidal safeners.

Grabiak's Compound:



wherein R is $C_{1\text{-}5}$ alkyl, phenyl or benzyl

Howe's (prior art) Compound:



Note that when the R substituent is ethyl in the Grabiak compound, that the only difference in structure between Grabiak and Howe is a single atom, namely, an oxygen atom versus a sulfur atom. Hence, structural similarity and identical utility on its own cannot be the sole basis for a rejection under 35 U.S.C. § 103. Yet, the Examiner's rejection in the instant application under 35 U.S.C. §103 does just that, except that in the instant case, the Blum et al. reference is one step further moved than in the Grabiak case since there is only structural similarity.

Based upon the foregoing, the rejection of claim 18 under 35 U.S.C. §103(a) over Blum et al. is obviated and should be withdrawn.

The Examiner has rejected claim 18 under 35 U.S.C. §103(a) as allegedly being unpatentable over Mitra et al. The Examiner alleges that compounds that are analogues, homologues or ring position isomers of the prior art compounds which Applicants have excluded by proviso are embraced by Applicants' claim 18 and render claim 18 obvious. Applicants respectfully traverse this rejection.

The Examiner has not established a *prima facie* case of obviousness. As discussed above in the traversal of the rejection of Claim 18 under 35 U.S.C. §103(a) over Blum et al., in order to establish a *prima facie* case of obviousness, first there must be some suggestion or motivation to modify the reference. The reference does not provide any suggestion or motivation to modify Mitra et al. to arrive at Applicants' genus. Second, there must be a reasonable expectation of success. Mitra et al. is directed to use of compounds as fungicides, whereas the instant application is directed to compounds and their use as inhibitors of protein kinase activity, an entirely different and unrelated use. One of ordinary skill in the art of medicinal chemistry would not expect a fungicide to be an effective inhibitor of protein kinase actvity.

An invention is to be considered as a whole. That is, in this case, does Mitra et al. make obvious the entire genus of any of Applicants' claims? As discussed above in the traversal of the rejection of claim 18 under 35 U.S.C. §103(a) over Blum et al., numerous cases support that all of the claim limitations must be taught or suggested by the prior art, and that there must be adequate support in the prior art for any change in structure over the prior art. Further, the invention is to be considered as a whole, not parsed out into its individual components.

The Examiner cites as examples "A compound wherein $R^1$ is methyl and R is 2-hydroxy-3-chlorophenyl embraced by the claim is rendered obvious by the prior art compound wherein R1 is methyl and R is 2-hydroxy-3-bromophenyl (one halogen renders the other obvious)", "A compound wherein $R^1$ is methyl and R is 4-hydroxy-3-bromophenyl embraced by the claim is rendered obvious by the prior art compound wherein $R^1$ is methyl and R is 2-hydroxy-3-bromophenyl (ring position isomer)" and "A compound wherein $R^1$ is ethyl and R is 2-hydroxy-3-bromophenyl embraced by the claim is rendered obvious by the prior art compound wherein $R^1$ is methyl and R is 2-hydroxy-3-bromophenyl (methyl versus ethyl). Applicants do not have claims to the species suggested by the Examiner. Applicants' claim 18 is a genus claim. Nonetheless, the question at issue is whether the invention as a whole would be obvious, not whether individual

differences between the prior art and the claims would be obvious. The fact that a claimed species or subgenus is encompassed by a prior art genus is not sufficient by itself to establish a *prima facie* case of obviousness. In re Baird, 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994). Thus, Mitra et al. does not establish a *prima facie* case of obviousness as to the entire genus of Claim 18.

Based upon the foregoing, the rejection of claim 18 under 35 U.S.C. §103(a) over Mitra et al. is obviated and should be withdrawn.

The Examiner rejected claims 18-21 and 23-45 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants' response to the Examiner's enumerated points are numbered accordingly to track the Examiner's points.

iii) With respect to the term "substituted", Applicants have amended claims 18, 37 and 39 to list suitable substituents for R, $R^3$, $R^4$ and $R^5$. Support for these amendments can be found, *inter alia*, on page 12, lines 10-26.

iv) Regarding claims 28-36, in Applicants' prior response to the Examiner's allegation that it was unclear what is intended to be accomplished in claims 28-36 in which Applicants pointed to the portion of the instant specification, i.e. page 91, lines 16-24, which defined what the compound of the invention do, which is inhibit protein kinases from serine/threonine and tyrosine kinases class. The Examiner now states that the claims need to be limited to these protein kinases because the claim as presented is broader than the broadest description in the specification. Applicants have amended claim 28 to limit the kinases to those listed on page 91, lines 5 and 16-24 of the instant specification.

v) Regarding claim 29, without conceding to the correctness of the Examiner's rejections and for the sole purpose of expediting prosecution of the instant application and to place it in condition for allowance Applicants have cancelled claim 29.

Based upon the foregoing, the rejection of claims 18-21 and 23-45 under 35 U.S.C. §112, second paragraph, is obviated and should be withdrawn.

The Examiner has rejected claims 28-38 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter not described in the specification to enable one to make or use the invention. Applicants respectfully traverse this rejection.

Without conceding to the correctness of the Examiner's rejections and for the sole purpose of expediting prosecution of the instant application and to place it in condition for allowance,

Applicants have amended claim 37 to delete the term "hyperproliferative disorders". Applicants have further amended claim 37 to add "thyroid hyperplasia, Grave's disease, cysts, and polycystic ovarian syndrome", which are species of hyperproliferative disorders. Support for this amendment can be found, *inter alia*, on page page 90, lines 4-5 of the instant specification.

The Examiner states "No compound has shown clinical efficacy all cancers, thus no in vivo or in vitro assay could be validated for the identification of such a general agent. Applicants' specification logically must lack such assay data." Without conceding to the correctness of the Examiner's rejections and for the sole purpose of expediting prosecution of the instant application and to place it in condition for allowance, Applicants have amended claim 38 to delete the term "angiogenesis". Applicants have further amended claim 38 to add "arthritis, atherosclerosis, psoriasis, hemangiomas, myocardial angiogenesis, coronary and cerebral collaterals, ischemic limb angiogenesis, wound healing, peptic ulcer Helicobacter related diseases, virally-induced angiogenic disorders, fractures, Crow-Fukase syndrome (POEMS), preeclampsia, menometrorrhagia, cat scratch fever, rubeosis, neovascular glaucoma, diabetic retinopathy, retinopathy of prematurity, age-related macular degeneration, solid tumors, malignant ascites, hemopoietic cancers, Herpes simplex, Herpes Zoster, AIDS, parapoxvirus, psoriasis, Kaposi's sarcoma, protozoan infections and toxoplasmosis, endometriosis, ovarian hyperstimulation syndrome, preeclampsia, systemic lupus, sarcoidosis, synovitis, inflammatory bowel disease, Crohn's disease, sickle cell anaemia, Lyme's disease, pemphigoid, Paget's disease, hyperviscosity syndrome, Osler-Weber-Rendu disease, chronic inflammation, chronic occlusive pulmonary disease, asthma, rheumatoid arthritis and osteosarthritis". These diseases have angiogenic components which can be affected by inhibition of protein kinase activity. Support for this amendment can be found, *inter alia*, at page 89, lines 21 to page 90, line 3 and page 93, line 20 to page 94, line 1 of the instant specification.

With respect to the method of claims 28-36, the benefit of inhibiting protein kinase activities *in vitro* is to test for pharmaceuticals or diagnostics as well as to initially estimate therapeutic dosages. Inhibiting protein kinase activities in mammals with below normal protein kinase activities or asymptomatic mammals with upregulated protein kinase activities would be beneficial because such inhibition would regulate and modulate abnormal or inappropriate cell proliferation, differentiation or metabolism, as stated on page 28, line 24 of the instant specification.

The Examiner asks "Is extensive experimentation required on the part of a potential infringer to determine if his use of Applicants' inhibitor falls within the limitations of applications claim?' In re Kirk and Petrow, 153 USPQ 48 (CCPA 1967)." In In re Kirk and Petrow, the issue with respect to 35 U.S.C. §112 was that the specification contained no specific statement as to how the claimed compounds were useful. The therapeutic properties of the compounds were stated in general terms such as "useful biological properties". This is not the case in the instant application. In the instant application Applicants have explained the functions of different protein kinases and how the activity of those protein kinases affect hyperproliferative disorders, inflammatory diseases and angiogenesis. Applicants have further explained how diseases and disorders with hyperproliferative, inflammatory or angiogenesis components can be affected by the inhibition of protein kinase activity and have given numerous examples of specific diseases and disorders in which inhibition of protein kinase activity would be useful. Applicants have clearly defined how their compounds can be used by listing diseases in which they can be used as well as detailing pharmaceutical formulations and dosage information on page 95, line 18 through page 105, line 5 of the instant specification. Applicants have given examples of which protein kinase activities are inhibited and have provided assays to test for inhibition of protein kinase activity. It would be routine experimentation in the field of medicinal chemistry to subject a compound to these assays.

With respect to the Examiner's quotation of Brenner v. Manson, 148 USPQ at 696: "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion", Applicants submit that the Examiner has taken the quotation out of context. Brenner v. Manson concerned an application for a product by process for which no utility was disclosed for the product. This differs from the instant case wherein specific compounds are disclosed as well as numerous practical applications for them, i.e. many diseases and disorders in which the compounds can be used. Immediately following the quotation cited by the Examiner, Brenner v. Manson proceeds to cite Application of Ruschig, 52 CCPA (Pat.) 1238, 1245, 343 F.2d 965, 970 "[A] patent system must be related to the world of commerce rather than to the realm of philosophy...". The instant application is grounded in the world of commerce in that it is directed to therapeutics which can be used to treat diseases. It is not directed to compounds with no known utility. In fact, Applicants list numerous specific diseases and disorders in which the claimed compounds can be utilized.

The Examiner states "As U.S. Court of Customs and Patent Appeals stated In re Diedrich 138 USPQ at 130, quoting with approval from the decision of the board: 'We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.' Applicants respectfully point out that In re Diedrich concerned a case in which the appellant stated his compounds were "useful for technical and pharmaceutical purposes." Not only did the appellant fail to provide a specific utility for his compounds, but upon appeal the appellant argued that the compounds could be used as X-ray contrast agents and proceeded to cite numerous patents which disclose compounds similar to his as being useful as X-ray contrast agents. The CCPA found that appellant's disclosure failed to satisfy the demands of 35 U.S.C. §112. On the contrary, in the instant case Applicants have provided specific uses for their compounds, i.e. inhibiting protein kinase activity, shown how to measure the inhibition of the protein kinase activity, i.e. providing assays used to test compounds, and listed specific diseases in which the inhibition of protein kinase activity would be beneficial. Applicants have not provided a vague or undefined use for their invention but have instead provided a detailed explanation of how the inhibition of protein kinase activity can be used in a therapeutic context.

Based upon the foregoing, the rejection of claims 28-38 under 35 U.S.C. §112, first paragraph is obviated and should be withdrawn.

The Examiner has rejected claim 18 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner points to the proviso that excludes a compound and reads "provided that when $R^1$ is methyl, R is not hydroxymethl, nitrophenyl, m-$OCH_3C_6H_4$, 4-hydroxy-3-methoxyphenyl or 2-hydroxy-3-bromophenyl." The Examiner alleges that these provisos lack description in the application as originally filed. Applicants respectfully traverse this rejection.

The Examiner cites Ex parte Grasselli. In Ex parte Grasselli, the Applicant added limitations to a claim to overcome prior art and the claims were subsequently rejected uner 35

U.S.C. 112, first paragraph, for lack of description. Ex parte Grasselli involved the way Grasselli attempted to avoid the prior art, namely by adding a negative limitation that in effect broadened the scope of the original claim. In point of fact, the Board stated "[i]t might be added that the express exclusion of certain elements implies the permissible inclusion of all other elements not so expressly excluded". Ex parte Grasselli, 231 USPQ 393, 394 (Bd. App. 1983). The holding of the Board had more to do with the way the negative limitation was worded so that the claim at issue actually claimed more than it originally did. Further, the Board stated that the negative limitations added new concepts. This is not the same as the situation in the instant application. The provisos in Applicants' claim specifically carve out compounds that were in the prior art. The provisos result in a narrower scope of the original claim and do not result in the inclusion of new elements that are not specifically excluded. No new concepts are raised by the addition of the proviso to claim 18. In fact, the invention is the same as was originally described; Applicants have merely excluded specific compounds. In fact, claim 18 is narrowed by the addition of the proviso. Therefore, the proviso does not give rise to the same issue that the Board in Ex parte Grasselli held against.

Further, in support of the provisos, Applicants direct the Examiner's attention to *In re Edward*, 568 F 2d 1349, 1351- 1352 (CCPA 1978), which supports Applicants' position that ipsis verbis disclosure is not necessary to satisfy the written description requirement of 35 USC 112 ¶1. See *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1570 (Fed. Cir. 1996);' *In re Edwards,* 568 F.2d 1349, 1351-52 (CCPA 1978) (asserting that all that is required is that the Application reasonably convey to persons skilled in the art that, as of the filing date, the inventor had possession of the subject matter later claimed by him). Furthermore, inquiry into the question of whether a particular claim complies with the written description requirement of 35 USC 112¶1 is a factual one that must be assessed on a case-by-case basis. See Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1562 (Fed. Cir. 1991) (reviewing with approval a line of CCPA cases that stressed the fact specificity of inquiries regarding compliance with the written description requirement of 35 USC 112¶1).

Applicants respectfully contend that the proviso in the previous Response does not undermine the claim's patentability vis-a-vis the written description requirement of 35 USC 112¶1 because the mere lack of literal support for the proviso in the application as filed is insufficient to support the Examiner's rejection. See *In re Edwards*, 568 F.2d 1349, 1354 (CCPA 1978) (holding that the USPTO must also supply reasoning as to why a claim lacking literal support fails to comply with the written description requirement of 35 USC 112¶1).

Furthermore, the Applicants respectfully contend that the application, at the time it was filed, would have reasonably conveyed to one of ordinary skill in the arts of organic and medicinal chemistry that the Applicants were in possession of the subject matter of claim 18 as amended because the amended claim reads on the bulk of the exemplification provided in the application. See *In re Johnson*, 558 F.2d 1008, 1019 (CCPA) (stating"[t]he notion that one who fully discloses, and teaches those skilled in the art how to make and use, a genus and numerous species therein, has somehow failed to disclose, and teach those skilled in the art how to make and use, that genus minus two of those species, and has thus failed to satisfy the requirements of [35 USC] 112, first paragraph, appears to result from a hypertechnical application of legalistic prose relating to that provision of the statute"). Additionally, the Applicants respectfully assert that because the application, at the time it was filed, supported claim 18 as originally filed, i.e., prior to its amendment to include the proviso, the application, at the time it was filed, necessarily supports claim 18 as amended. See *In re Johnson*, 558 F.2d 1008, 1019 (CCPA) (holding that "the specification, having described the whole, necessarily described the part remaining").

Adequate description under the first paragraph of 35 U.S.C. § 112 does not require literal support for the claimed invention. *In* re *Herschler*, 591 F.2d 693, 200 USPQ [*5] 711 (CCPA 1979); *In re Edwards,* 568 F.2d 1349, 196 USPQ 465 *(*CCPA 1978*); In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976). Rather, it is sufficient if the originally-filed disclosure would have conveyed to one having ordinary skill in the art that an applicant had possession of the concept of what is claimed. *In re Anderson*, 471 F.2d 1237, 176 USPQ 331 (CCPA 1973).

The patent law provides for the amendment of claims during prosecution. To proviso out specific compounds has been a long accepted practice within the USPTO. Literal support for a proviso excluding specific compounds has not previously been required. So long as an applicant conveys that he had possession of the invention at the time of filing he has met the requirements of 35 U.S.C. § 112, first paragraph.

Applicants' written description clearly conveys that Applicants had possession of the instant invention at the time of filing. One of ordinary skill in the art of medicinal chemistry would understand the written description and claims as filed by Applicants, as well as the amended claims. The application as originally filed provided adequate written description for the claims as originally filed. The proviso inserted by Applicants merely excises a small group of compounds. It does not change the nature of the instant invention. Since a narrower breadth is encompassed by the original claim, and the application as originally filed provided adequate

written description for the originally-filed claims, it follows that a claim of narrower scope is necessarily supported. Therefore, the instant specification provides the requisite evidence of possession for amended claim 18.

Based upon the foregoing, the rejection of claim 18 under 35 U.S.C. §112, first paragraph, is obviated and should be withdrawn.

No fees are due for the instant amendment since the total number of claims after entry of the amendments hereinabove is not more than the total number of claims that Applicants have paid for to date.

Based upon the foregoing, Applicants believe that claims 18-21 and 23-39 and 41-45 are in condition for allowance. Prompt and favorable action is earnestly solicited.

If the Examiner believes that a telephone conference would advance the condition of the instant application for allowance, Applicants invite the Examiner to call Applicants' agent at the number noted below.

Respectfully submitted,

Date: February 13, 2004

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